

Asymmetric stent containing irregularly distributed active agents or radioisotopes useful e.g. for treating atherosclerosis and preventing restenosis

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Abstract of DE19913978

Asymmetric stents have asymmetry due to geometric shape, irregular distribution of drugs (I) and/or carriers for (I), variation in the nature of a polymeric coating, variation of (I) release properties or irregular distribution of chelated radioactive ions. Asymmetric stents are claimed, in which: (A) (i) there is no plane of symmetry perpendicular to the stent axis at the center of the stent and/or along the stent axis; (ii) there is no center of symmetry at the center of the stent; (iii) the shape does not consist completely of regularly repeating or sequenced symmetry elements; (iv) fractal geometry is shown; and/or (v) the stent tapers from one end to the other; (B) conditions (A) (i)-(iii) do not apply and the surface of the stent is provided with one or more (I) carrying or releasing carrier(s), where the carriers and/or their properties are non-homogeneously distributed over the stent; (C) the stent contains one or more (I), the concentration, nature, ratio and/or release rate of which is not constant; (D) the stent has one or more polymer layer(s) (optionally incorporating or surface coated with (I)), where one or more of the type of polymer, the layer thickness and/or density and the concentration, nature and ratio of (I) is/are not constant or (E) radioactive ions are fixed to chelate formers on the surface of the stent and the distribution of radioactivity is non-homogeneous. Independent claims are included for methods for producing asymmetric stents (including asymmetric radioactive stents).

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The invention is on the area of the container implants and describes asymmetrical Stents, procedures for its production and its use to the remainder eye prophylaxis.

State of the art

Stents are state of the art (Psyhyrembel, clinical dictionary 257. Edition, publishing house W. de Gruyter). Stents are endoprostheses, which make keeping possible course-like structures open in bodies of humans or animals (z. B. Container, Ösophagus, trachea, Gallengangstent). They become as palliative measure with narrowings by catch (z. B. Atherosklerose) or pressure from the outside (z. B. with tumors) uses. Stents are made usually of high-grade steel or nickel/titanium alloys (Nitinol) and are regularly formed, D. h. they consist of constantly repeating homogeneous components. This means that they exhibit a high symmetry. They are z. B. mirror-symmetrically concerning a mirror plane (C2v-Symmetrie), thought by the Stentmitte perpendicularly to the Stentachse, and/or symmetrically to in the Stentachse running mirror plane, which besides still at will can be rotated (D INFINITY h-symmetry). In addition they can be point symmetrical concerning the Stentmittelpunkt. The point symmetry can occur additionally to the mirror symmetry or be the only symmetry element.

Stents are described and become clinical after container-surgical or interventional radiological interferences (z. B. Ballonangioplastie) to the remainder eye prophylaxis tested. They are even, D. h. homogeneous or in all places of the Stents homogeneously, with a polymer coats, which contains the active substance evenly distributed.

Active substance-containing or active substance-setting free Stents usually contain into a polymer layer trained active substances, z. B. Medicament, which either directly from the surface to work or those to be gradually set free be able and the remainder eye to prevent be supposed. The coating of the Stents takes place in homogeneous way. This means that the Stents in all places evenly and with same speed releases or in the surface for effect holds the active substance ready.

This uniformity and/or. high symmetry of the Stentgrundkörpers or its coating does not correspond however to the physiological conditions of its operational area. Stents are implanted preferentially in body cavities, particularly into blood vessels, which are characterized thereby that they exhibit a preferred direction, z. B. the direction, in which the blood or the Galle flows (Gefäßstents and/or. TIP of implants) or the direction of flow of food (implantation into the esophagus). The conventional Stents does not do justice to these vector characteristics of the operational area. Now is to be considered to the vector characteristics, in order to provide the Stents thereby more effectively, better compatible and - in case of the Gefäßstents - with less inclination to the remainder eye by the new form and/or coating.

In the following all Stents becomes, those in its form and/or coating deviates from the highly symmetrical form of conventional Stents with C2v-Symmetrie, D, described above, INFINITY h-symmetry and/or point symmetry and/or. with constantly repeating local symmetry components (see. Fig. 1) ?asymmetrical Stents? or ?asymmetrical Stents? calls. Such Stents was so far not described.

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Task of the available invention is it to make Stents available more effective and better compatible is than conventional Stents. This task is solved by those in the following described Stents, as they are characterized in the patent claims.

Description of the invention

The task described above is solved according to invention by the fact that the Stents is not as before completely symmetrical any more, but from this symmetry deviating characteristics to exhibit. This is reached by the fact that the form and/or the characteristics of the Stents, z. B. their surface, is asymmetrical and/or. exhibit a reduced measure of symmetry compared with the conventional Stents. A development of these characteristics is exemplarily being present vector characteristics concerning the form of the Stents. Alternatively - also the surface (highly more symmetrical or more asymmetrical) can be modified Stents such that it is not identical for all points of the surface, D. h. a possible however not necessarily necessary surface modification is not highly symmetrical but asymmetrical and/or. less symmetrically on the Stent distributes. Symmetrically it means in this connection that itself geometrical arrangements, z. B. the Stentstreben or a possible coating, in regular way repeat steadily. Asymmetrically it means that the regular arrangement of geometrical arrangements and/or coatings and/or concentrations and/or the release rates of active substances or modifying Agenten is not present any longer. Exemplarily conventional Stents is symmetrical concerning a mirror plane, which runs perpendicularly to the Stentachse. With a special development of the new Stents the symmetry is given no more concerning a mirror plane perpendicularly to the Stentachse. This can mean either that the Stent of an end tapers itself on the other hand and/or that itself the form or arrangement of construction units, z. B. the bracings, by the one on the other hand end changed, in a special development can be replaced also only the regular repetition of arrangements by an irregular arrangement.

It continues to be also conceivable that the form of the Stents exhibits fraktale geometry or fraktale characteristics

exhibit the surface of the Stents.

The device according to invention consists thus in this development of a Stentgrundkörper, which compared with the available Stents a modified or reduced symmetry exhibits and/or whose surface in all two dimensional elements is not identical, by z. B. the coating with a polymer in different places of the polymer is different or the local concentration of a trained or set free active substance, z. B. a medicament, in different places of the Stents is not alike.

The form of the new Stents can be varied at will, only condition is that it compared with the conventional Stents a modified and/or. If symmetry reduced, prefers an arranged (vector) symmetry exhibit. The deviation from the symmetry usual Stents is possible in several kinds. On the one hand the deviation is feasible by modification concerning a symmetry plane, which runs exemplarily perpendicularly to the Stentachse. In addition, it is possible to modify the symmetry concerning one level which runs in the Stentachse. Both possibilities are exemplary in fig. 2 compared with a conventional symmetrical Stent represented. The production of the new Stents can take place in the same way as for the now common Stents. The production from individual wires, which are into one another interlaced, is conceivable, as this is accomplished for the Strecker Stent. Alternatively the Stents can be cut out also computer controlled of a pipe, z. B. by means of laser technology. Examples of the new Stents are possible in various way by modification of symmetry planes and/or modification or distance of individual symmetry elements of the current symmetrical Stents. Some examples are in fig. 3 represented.

A further development of the invention is based to modify the surface of symmetrical Stents asymmetrically. This means that there are ranges on the Stents, which differ from other ranges according to their surface. This distinction refers however not to each individual point of the Stents separates to ranges of same symmetry, as they are inevitably by the structure of the Stents from bracings given.

The surface of the Stents can deviate optionally from the one normal metal surface by modification or coating. The coating knows either homogeneously, D. h. at all points of the surface homogeneously and/or, evenly its, if it concerns asymmetrical Stentgrundkörper, or - are conventional with symmetrical Stents, as it used, - then the coating must and/or. Surface modification asymmetrically and/or. less symmetrically or arranged its. Possible also the combination of asymmetrical Stentgrundkörper is + asymmetrical surface modification.

For surface-modified Stents the commercial Gefäßimplantante can be used, z as bases. B. a Wiktor Stent, a Strecker Stent, a Nitinol Stent or a Palmaz treasure Stent. The Stentgrundkörper can be made of a polymer metallically or.

The surface can be coated with a polymer, active substances release, even an active substance represent or at its outside layer bound contained can. With the active substances it can concern also around medicaments or radioactive substances or metals. Likewise the radioactive substances or metals can be applied also directly on the Stent, without additional polymer. Crucial distinguisher to all Stents used so far is however old points identical the condition of the surface not at and/or. not in all points of the surface same concentration of active substances and/or release rate of active substances.

When carrier polymers come all polymers, for example PU, described so far for the coating of Stents, Polyactide, Polyglycolide as well as copolymers in consideration, into which active substances can be embedded. In addition, modified PU be possible, which carry derivatisierbare groups, can, to which for that or the active substances kovalent be bound can. As polymers therefore z are possible. B. Polyethylenglycole, Polysaccharide, Cyclodextrine or Polyaminopolycarbonsäuren, those as derivatisierbare groups of revision modification NO, hydroxyl, carboxyl, Carbonyl, Thiol, Thio-carboxyl or other functions, which can be converted, contain.

There is in addition, polymers on the basis of funktionalisierten Poly p xylienen like z. B. Polyamino p xylen (formula I) favourably as carrier polymers applicable.

EMI6.1

Further the following polymers can be used as carrier polymers:

Polyorganosilane, Poly N vinylpyrrolidon, polymethyl metacrylate, Polyhydroxymethylmethacrylat, copolymers from N-Vinylpyrrolidon and Hydroxymethylmethacrylat, PP, Polyacrylamid, polyethylene, polyethylene oxide, polyester, polypropylene oxide, PVC or PVC derivatives, Polyvinylactam, polyethylene terephthalate, polysulfone or Polysulfonat.

The Stents according to invention can be manufactured exemplarily as follows:

1. A Metalstent, z. B. a Streckerstent, is made of individual wires, as this admits to the specialist is. In contrast to the past procedure the Stent however no more in a symmetrically repeating sample at junction points manufactured to separate with alternating samples.
2. Cut from a high-grade steel pipe by means of laser technology in the conventional and the specialist trusted way a Stent. The new form differs from the past by its non-symmetry concerning a mirror plane, which runs perpendicularly to the Stentebene. This means that z. B. the bracings to end of the Stents differently run than at the other end.
3. Cut from a high-grade steel pipe by means of laser technology in the conventional and the specialist trusted way a Stent. The new form differs from the past by the fact that the bracings in the center section of the Stents run differently (shows another arrangement) than the bracings at the two ends of the Stents.
4. Cut from a tapering high-grade steel pipe by means of laser technology in the conventional and the specialist trusted themselves way a Stent. The new form differs from the past by the taper ratio of the Stents.
5. Of Nitinol an expanding Stent in that the specialist trusted way made, or several of the characteristics specified under 1-3, z. B. Taper ratio, change of the symmetry of the one on the other hand end, exhibits.
6. Uncoated Stent asymmetrical symmetrical in the form or can first with a carrier polymer (z. B. a PU, available from the reaction of a amphiphilic Polyethers, Diphenylmethan-4-4' to be diisocyanat and Butandiol) coated. This polymer is so modified that it at the surface derivatisierbare groups, z. B. Amino, hydroxyl or groups of carboxyls carry. The polymer becomes in a solvent (z. B. Chloroform) solved and the Stent into the polymer solution dried in. After withdrawal of the Stents from the polymer solution it is dried in a baking oven at ambient temperature. Alternatively to

if the carrier polymer can be applied with the help of the gaseous phase separation or the plasma polymerization on the Stent. This procedure is based to z. B. on the procedure for the production of antithrombogenic surfaces on medical articles, revealed in the German disclosure writing DE 196 04 173 A1. With this procedure a funktionalisiertes polymer is applied by gaseous phase coating at increased temperatures and reduced pressures on the metallic Stentgrundkörper. After 1. or 2. coated Stent becomes with a solution of the Derivatisierungsmittels, z. B. DTPA Dianhydrid shifts. The proceeding is well-known the specialist. Subsequently, the asymmetrical conversion with a radioactive metal isotope takes place. In addition the Stent can in each case with the ends into a solution of a radioactive metal salt, z. B. Re-188-Nitrat, to be divided in, whereby the center section is not immersed. After a washing process the entire Stent is immersed into a solution by calcium chloride. Now the Chelate at the two ends contain Re-188 and the center section are free from radioactivity. Alternatively also only one end radioactively or only the center section can be made. This takes place via choice of the sequence of immersing. Alternatively to calcium also radioactive rhenium cannot know used and by suitable choice of immersing arbitrary parts of the Stents to be radioactively marked. A condition is in all cases that in the form symmetrical Stents is asymmetrisch coated, while in the form asymmetrical Stents can be also symmetrisch coated.

7. Uncoated Metallstent asymmetrical symmetrical in the form or at his surface by removing the oxide coating by means of acid one activates. Subsequently, the Stent is immersed into the solution of a radioactive metal salt (containing radioactive metal ions). The radioactive metal separates at the surface of the Stents. Asymmetrical coating is possible in several kinds. Once only one part of the Stents, z. can B. afterwards the two ends, from the oxide coating to be released (by immersing these parts into the acid) and with radioactive metal to be coated. In addition, on the other hand activation and following deactivation steps can be repeated, so that 7sample? determined at separated metal on the Stent be produced can. Deactivation (production of an oxide coating, on which radioactive metal cannot separate) takes place via immersing the Stents or Stentteile into oxidizing solution z. B. Hydrogen peroxide, potassium permanganate, manganese dioxide, etc. The procedure is revealed in the registration WERE to 98/48 851.

8. Alternatively also the oxide coating of a metallic Stents can be derivatisiert after breaking open with acid with chlorosilanes. This Derivatisierung takes place asymmetrisch such that only parts of the Stents are derivatisiert, while the other parts remain underderivatisiert. If the chlorosilanes finalconstant, possibly. protected active groups, z. B. Amino groups, carry, can these amino groups afterwards with complexing agents be converted further, like this under 6. is already described. The Stent can be provided then by this process with an asymmetrical radioactive surface.

9. Symmetrical or asymmetrical Metallstents can be provided also with a carrier layer, the active substances (z. B. Medicine materials) contains. Several possibilities are given. Symmetrical Stents is provided with a carrier layer, which is asymmetrisch arranged and/or not in all places equal to Stents is and/or the same concentration at active substance does not contain and/or does not exhibit the same release rate for the active substance.

The necessary processing steps for the execution above of the procedures described in principle are well-known the specialist. Special execution forms are in detail in the examples described.

The Stents according to invention solves the initially described task. The Stents according to invention is physiologically well compatible.

Fig. 1 shows schematic examples of from identical local symmetry elements (8squf8) developed highly symmetrical Stents. That filled out drawn local symmetry element does not mean that the Stentsstreben is closed. It is to represent only the marking of a symmetry component, which constantly repeats itself. The symmetry element can be also asymmetrical in itself, D. h. no mirror planes or points of mirror exhibit.

Fig. shows 2 examples of symmetrical (A-B) and for 7asymmetrical? Stents (CC).

Fig. 3 a schematic example of one shows only at the ends (8squf8) modified, in the form highly symmetrical Stent. Filled out the drawn local symmetry elements therefore do not mean that the Stentsstreben is closed. This Stentsabschnitt can contain another carrier and/or another surface and/or another active substance and/or another active substance concentration and/or another release rate for the active substance and/or consist of another material than the middle Stentsabschnitt.

Fig. shows 4 a schematic example of at a half (8squf8) modified, in the form highly symmetrical Stent. Filled out the drawn local symmetry elements therefore do not mean that the Stentsstreben is closed. This Stentsabschnitt can contain another carrier and/or another surface and/or another active substance and/or another active substance concentration and/or another release rate for the active substance and/or consist of another material than the middle Stentsabschnitt.

Fig. 5 is a representation, with which the asymmetrical structure of the new Stents is schematically pointed out.

Remark examples

The following examples are to describe the invention article, without wanting to limit it to these.

Example 1

Uncoated Stents - I

Stents are cut by means of lasers from a high-grade steel pipe. The form of the Stents is characterized by the fact that they are not concerning one perpendicularly to the Stentebene thought mirror plane symmetrical. Stents are manufactured, which begin at an end with a close network of props, which receives on the other hand end ever larger distances between the props.

Example 2

Uncoated Stents - II

Stents are cut by means of lasers from a Nitinolrohr. The arrangement of the Stentsstreben is characterized by the fact that it runs at the two ends of the Stents differently than in the center of the Stents. The 7density? of the props is larger at the ends than in the center section of the Stents.

Example 3

Uncoated Stents - III

Stents are cut by means of lasers from a Nitinolrohr. The arrangement of the Stentstreben is characterized by the fact that it runs at the two ends of the Stents differently than in the center of the Stents. The density of the props is smaller at the ends than in the center section of the Stents.

Example 4

Uncoated Stents - IV

Stents cut themselves by means of laser technology from a tapering high-grade steel pipe. The arrangement of the Stentstreben takes place after a repetitive, even sample.

Example 5

Uncoated Stents - V

Stents cut themselves by means of laser technology from a tapering Nitinolrohr. The arrangement of the Stentstreben takes place after a repetitive, even sample.

Example 6

Uncoated Stents - VI

Stents cut themselves by means of laser technology from a tapering Nitinolrohr. The arrangement of the Stentstreben takes place after a sample changing from one on the other hand end.

Example 7

Stents with chelating agents at the surface - I

A Stent is coated with a carrier polymer, as it is familiar the specialist. As carrier polymer PU is used, which is available by reaction of an amphiphilic Polyethers, Diphenylmethan-4,4' disocyanat and Butandiol as the chain-longer. In order to increase the yield at couplingable groups, also additional functions can, like z in the individual components. B. Amino groups, contained its, which can be present during the polymerization possibly protected. The Stents is coated by the fact that they are immersed into a 5% chloroform solution of the polymer. Afterwards one lets it dry to a pure space baking oven at room temperature. The average layer thickness amounts to 20 µm. The Derivatisierung with chelating agents takes place via conversion of free amino groups with the until anhydride from DTPA, how it is common in the literature described and the specialist. After the Trocknung becomes the Stent in each case at the two ends (1/4 the Stentlänge) into a solution of a not radioactive metal salt, z. B. Iron perchloride, manganese chloride, rhenium chloride etc. dived in, so that the Metallchelate a Metallion can komplexieren. The entire Stent becomes subsequently, into a solution of a radioactive metal salt, z. B. Re-188 chloride dived in. The center section of the Stents not saturated yet so far with metal ions takes up now the Re-188-Ionen. The two Stentenden, which already komplexiert non radioactive metal ions, are not any more able, further, to take up radioactive metal ions. After drying the Stent is ready for use. It now exclusively contains in the center radioactive metal ions. The radioactive range of the Stents is simply controllable thereby how deeply the two Stentenden were immersed before into a solution with non-radioactive metal ions.

Example 8

Stents with chelating agents at the surface - II

A Stent becomes, as in Example 6 described, coated with a polymer with reactive amino groups and afterwards with complexing agents derivatisiert. In such a way prepared Stent is immersed in each case at the ends (1/4 the Stentlänge) into a solution with radioactive In-111-Chloride. The complexing agents take up thereby radioactive metal ions. Afterwards the Stent is washed with water and dived in completely into a solution with calcium chloride. After washing the Stent is ready for use. It exclusively contains at the ends radioactivity. The extent (the concentration and distribution on the Stent) is steered by submergence and the concentration of the radioactive metal ions in the Stent.

Example 9

Stents with chelating agents at the surface - III

A Stent becomes, as in Example 6 described, coated with a polymer with reactive amino groups and afterwards with complexing agents derivatisiert. Effected from radioactivity as in Example 7 it described an applying with the exception that the Stent is immersed after the first step (brings in of radioactive Re-188-Ionen at the ends to 1/4 the Stentlänge) into the solution of a gamma emitter (metal ions with gamma radiation). The Stent contains now at the ends (1/4 the Stentlänge) a beta emitter and in the center a gamma emitter.

Example 10

Stents with chelating agents at the surface - IV

The coating of a Metalstents by CVD polymerization (CVD: Chemical Vapour deposition) of 4-Amino [2,2] - paracyclophan effected in one suitably connected plant. The plant is connected with an argon bomb, since argon functions as feed gas. The argon inlet is with a 380 mm is enough for quartz glass pipe connected with an outside diameter by 30 mm. The quartz glass pipe is connected at its other end with a high-grade steel recipient. The quartz glass pipe is freely floating in a three-zone roaring furnace stored, which possesses a heated length of 320 mm and an inside diameter of 32 mm. All three heating zones can be heated up to 800 DEG C. The Stent which can be coated is fixed over the removable sediment bowl on the sample holder. Subsequently, the reactor is locked again and the plant is taken by manipulation of the main switch in enterprise. At the same time the two cooling circuits are activated, and the recipient wall is heated on 100 DEG C. Then a porcelain boat with a weighed quantity of monomer is placed into the sublimation zone and locked these again. The reactor is then evacuated on a basis pressure by 0.03 mbar. Now a feed gas stream of 20 is stopped afterwards sccm and an operating pressure is given by 0.2 mbar. One waits now so long,

until both the feed gas river and the operating pressure are constant. Now one gives the desired pyrolysis temperature of 680 DEG C and waits, until this temperature in the pyrolysis zone is reached. Then one lets the sample holder with a rotating speed of 20 rpm rotate and heats the sublimation zone up on 290 DEG C. The coating process is verified with the help of the layer thickness monitor. If the desired layer thickness is reached by 280 Nm, the coating process can be terminated. In addition the furnace automatic controllers, the Drehmotor of the sample holder and the feed gas stream are switched off, the throttle valve and evacuated again on basis pressure is opened. Subsequently, the pump is switched off, the plant over the ventilation valve is ventilated and the sample is taken. The Derivatisierung with complexing agents effected like already described by conversion of the free amino groups on the carrier polymer with DTPA Dianhydrid. After the Trockung takes place the conversion with a radioactive Metallion as described. In addition the Stent is immersed first afterwards at an end (1/4 the Stentlänge) into the solution one to gamma-ray-end metal ion, washed, and afterwards the remainder of the Stents into the solution beta ray-end one metal ion (z. B. Re-188-Nitrat) dived in. After washing and drying the Stent is ready for use and can be inserted alternatively with the gamma or the beta emitter ahead into the blood vessel.

Example 11

Stents with chelating agents at the surface - V

A conventional Nitinolstent is heated up in a 1N hydrochloric acid for 15 min on 80 DEG C. The oxide coating at the surface of the Stents is destroyed. Subsequently, in such a way pre-treated Stent is immersed in each case at the two ends (1/4 the Stentlänge) into a solution by Cl-SI (CH₃)₂ (CH₂)₄-NHCOCH₃ in dichloromethane. The Ti-OH-groups with the chlorosilane, developed at the surface, are derivatisiert. Subsequently, the acetyl group of the amine is removed and converted as in the examples with DTPA Dianhydrid, specified above. Subsequently, the further asymmetrical conversion with radioactive metal salts takes place as already described. The individual work procedures are the specialist trust.

Example 12

Stents with radioactive metal on the surface - I

A conventional Metallstent is immersed in hydrochloric acid. The oxide coating at the surface of the Stents is destroyed. In such a way pre-treated Stent becomes subsequently, in each case at the two ends (1/4 the Stentlänge) into a solution with oxidizing characteristics, z. B. Hydrogen peroxide, manganese dioxide, potassium permanganate or concentrated nitric acid dived in. In the places, which dive into the solution, the oxide coating is restored. The entire Stent becomes subsequently, into the solution of a radioactive metal salt, z. B. Re-188 chloride dived in. By separation of the nobler radioactive Metalles at the less noble metal of the Stents a layer from radioactive metal forms the Stentoberfläche at the parts of the Stents released from the oxide coating. The separation takes place however only in the places, which do not contain a metallic oxide (in the center of the Stents), thus not in the places, which by immersing into the oxidizing solution again oxidized (deactivated) are. After the drying process the Stent is ready for use.

Example 13

Stents with radioactive metal on the surface - II

A conventional Metallstent is immersed in each case at the two ends (1/5 the Stentlänge) in hydrochloric acid. The oxide coating at the surface of the Stents is destroyed. The entire Stent becomes subsequently, into the solution of a radioactive metal salt, z. B. Re-188-Chlorid dived in. By separation of the nobler radioactive Metalles at the less noble metal of the Stents a layer of radioactive metal at the surface of the Stents forms. The separation takes place however only in the places, which do not contain a metallic oxide (at the ends of the Stents), thus only in the places, which were activated by immersing in hydrochloric acid. After the drying process the Stent, which contains radioactivity only at the two ends (in each case 1/5 the Stentlänge), is ready for use.

Example 14

Stents with embedded active substance

A Metallstent is immersed perpendicularly into a solution, the one suspended or solved polymer, z. B. Polylactid, and a solved active substance, z. B. Iloprost and PEG Hirudin, contain. Subsequently, the Stent is pulled out of the solution. This procedure is several times repeated. The orientation of the immersing and pulling out procedure is always identical. Thus an asymmetrical coating of the Stents with low coating thickness develops to upper and high coating thickness at the lower end. After drying the Stent is ready for use.



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1. Asymmetrical Stents, by the fact characterized that its form on one level, those runs in the center of the Stents perpendicularly to the Stentachse and/or on one level, which runs in the Stentachse and/or cannot at a symmetry center in the center of the Stents not be reflected, and/or that their form is composed not exclusively of regularly repeating and/or symmetry elements in line and/or fraktale geometry exhibits and/or itself tapered by one on the other hand end.
2. Stents in accordance with requirement 1, by the fact characterized that they are provided with one or more active substance-basic and/or setting free carriers.
3. Stents in accordance with requirement 2, whereby the carriers and/or their characteristics are unevenly distributed over the Stent.
4. Stents, marked by it that their form on one level, which runs in the center of the Stents perpendicularly to the Stentachse can be reflected and/or on one level, which runs in the Stentachse and/or at a symmetry center in the center of the Stents, and/or whose form is composed of regularly repeating and/or symmetry elements in line exclusively, and whose surface with one or more active substance-basic or setting free carriers is provided, whereby the carriers and/or their characteristics are unevenly distributed over the Stent.
5. Stents, by the fact characterized that they contain one or more active substances, whereby the concentration and/or kind of the active substances and/or their mixing proportion and/or their release rate everywhere are not alike.
6. Stents, by the fact characterized that they contain one or more polymer layers with or without trained and/or on the surface bound active substances, whereby the kind of the polymers and/or their layer thickness and/or their density and/or the kind of the active substances and/or their concentration and/or their mixing proportion everywhere are not alike.
7. Stents in accordance with requirement 6, by the fact characterized that the distribution of active substances in a carrier layer is not identical in all places and/or their surface is asymmetrically (not evenly) coated and/or the concentration and/or release of active substances is not alike in each place.
8. Stents in accordance with requirement 6, by the fact characterized that the concentration and/or release of the active substance and/or, the active substances of the one on the other hand end increases.
9. Radioactive Stents, marked by it that radioactive ions are bound by chelating agents, which are fixed at the surface of the Stents, and that the distribution of the radioactivity on the Stent everywhere it is not alike.
10. Radioactive Stents in accordance with requirement 9, by the fact characterized that one or both ends do not contain radioactivity.
11. Radioactive Stents in accordance with requirement 9, by the fact characterized that the center section does not contain radioactivity.
12. Radioactive Stents in accordance with requirement 9, by the fact characterized that one or both ends contain higher radioactivity than the other parts of the Stents.
13. Radioactive Stents in accordance with requirement 9, by the fact characterized that the radioactivity of the one increases on the other hand end.
14. Stent in accordance with one of the preceding requirements, by the fact characterized that the Stentgrundkörper is made of metal or from a polymer of manufactured Stent.
15. Stent in accordance with one of the preceding requirements, by the fact characterized that the metallic Stentgrundkörper is a Wiktor Stent, a Palmaz treasure Stent, a Strecker Stent or a Nitinol Stent.
16. Stent in accordance with one of the preceding requirements, by the fact characterized that the carrier polymer is one of the following polymers: a Polylactid, Polyglycolid, a PU derivative, Polyamino p xylenderivat, a Organosilan, a n Vinylpyrrolidon, a Polyacrylat, a polymethyl metacrylat, a Hydroxymethylmethacrylat, a mixing polymer from N-Vinylpyrrolidon and Hydroxymethylmethacrylat, a PP, polyester, polycarbonate, Polysaccharid, a Polyacrylamid, a polyethylene, a polyethylene oxide, a Polyethylenglycol, a polypropylene oxide, a Tetramethyldisiloxan, PVC or a PVC derivative, a Polyvinylactam, a polyethylene terephthalate, silicone, polysulfone, a Polysulfonat or a mixture of the aforementioned polymers.
17. Procedures for the production asymmetrical radioactive Stents, by the fact characterized that a Metallstent is coated with a polymer, which contains reactive groups at its surface, to which a chelating agent is coupled, and which will provide asymmetrically with radioactivity by the fact that they are immersed not completely but only partially into a solution with one or more radioactive isotopes.

18. Procedure for the production asymmetrical radioactive Stents, by the fact characterized that radioactive isotopes are applied thereby on the surface by Metallstents that first the existing oxide coating is asymmetrically removed and that afterwards the radioactive isotopes are applied by separation at the places on the Stent, released from the oxide coating.
19. Procedure for the production asymmetrical radioactive Stents, by the fact characterized that radioactive isotopes are applied thereby on the surface by Metallstents that first the existing oxide coating at the two ends is removed and that afterwards the metal atoms of the Stents with reactive silanes are converted, the additionally reactive (protected first) groups contain, to which after Entschützung chelating agents can be coupled, which take up radioactive isotopes from a solution.
20. Procedure for the production of a active substance-coated Stents, by the fact characterized that the coating with carrier polymer takes place asymmetrically.
21. Procedure in accordance with requirement 20, by the fact characterized that the carrier polymer is applied by gaseous phase coating or plasma polymerization on the Stentgrundkörper.
22. Procedure in accordance with requirement 20, by the fact characterized that the carrier polymer is applied by repeated perpendicular immersing of the Stents in a solution or an emulsion or a suspension of a polymer and following pulling out on the Stent.
23. Procedure for the production of an asymmetrical Stents, by the fact characterized that the Stent is cut out of a pipe.
24. Procedure in accordance with requirement 23, by the fact characterized that the Stent is cut out of a high-grade steel pipe by means of laser technology.
25. Procedure in accordance with requirement 23, by the fact characterized that the Stent is cut out of a Nitinolrohr by means of laser technology.
26. Procedure in accordance with requirement 23, by the fact characterized that the Stent is cut out of a metal tube by means of laser technology and covered afterwards with a nobler metal.
27. Procedure for the production of an asymmetrical Stents, by the fact characterized that the Stent from one or more wires is twisted.


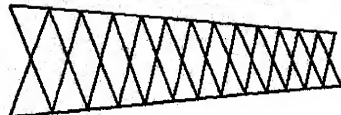
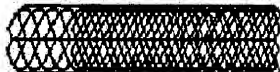
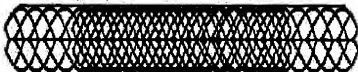
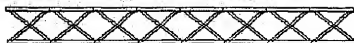
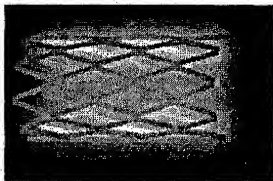


Abb. 2:



A

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C

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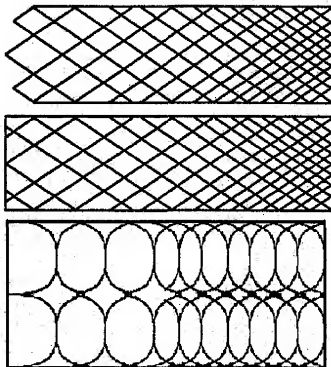
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Abb. 2 (Fortsetzung):



I

J

K

Abb. 3:

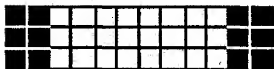


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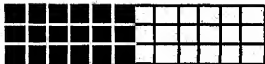


Abb. 5:

